REMARKS

Claims 20, 22, 23, 25-28, 30-31, and 33-34 have been amended. Claims 40-44 have been added. Support for the amendments and new claims can be found throughout the specification, including at page 6, lines 10-11; page 8, lines 2-5; page 15, line 23 to page 16, line 6; and page 16, lines 15-18. No new matter is added by the amendments. Claims 1-19, 21, 24, 32, 35, and 37-39 are canceled without prejudice or disclaimer. Therefore, claims 20, 22-23, 25-31, 33-34, 36, and 40-44 are pending in the application. Reconsideration of the claims in view of the following Remarks is respectfully requested.

35 USC § 102

Claims 17, 21, 23, 25-29, 34-35, and 39 were rejected under 35 USC § 102(e) as anticipated by Cleland. Claims 17, 21, 35, and 39 have been canceled. With respect to the remaining claims, Applicants traverse this rejection.

"A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference." *MPEP 2131* (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Moreover, even if the claims are subsumed by a prior art reference's generalized disclosure, the reference must provide guidance on how to construct a product having the advantages of the claimed product to be anticipating. *Minnesota Mining & Manufacturing co. v. Johnson & Johnson Orthopaedics, Inc.*, 24 USPQ2d 1321 (Fed. Cir. 1992).

The Applicants submit that Cleland does not anticipate the present claims. Amended claims 23, 25-29, and 34 depend from claim 22. Amended claim 22 recites an injectable formulation, comprising an injection vehicle comprising hyaluronic acid dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight by volume, and particles comprising a biologically active agent and a biocompatible polymeric matrix.

Cleland does not teach a formulation having all limitations of the claims. Cleland discloses polymeric microspheres comprising nerve growth factor, and states that:

> To prepare an injection using the microspheres obtained above, the microspheres may be formulated with a viscous physiologically acceptable solution; a dispersant (e.g., surfactants such as Tween-80, HCO-60; polysaccharides such as carboxymethylcellulose, sodium alginate, sodium hyaluronate....) (column 19, lines 47-53).

Cleland nowhere discloses, however, an injectable formulation as claimed, comprising hyaluronic acid dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight by volume. Applicants submit, therefore, that claims 23, 25-29, and 34 are patentable over Cleland. Withdrawal of the rejection is respectfully requested.

Claims 17, 21, 23, 25-28, 34 and 39 were rejected under 35 USC § 102(e) as anticipated by Suzuki. Claims 17, 21, and 39 have been canceled. With respect to the remaining claims, the Applicants traverse this rejection.

Amended claims 23, 25-28, and 34 depend from independent claim 22. Amended claim 22 recites an injectable formulation, comprising an injection vehicle comprising hyaluronic acid dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight by volume, and particles comprising a biologically active agent and a biocompatible polymeric matrix.

Suzuki does not disclose an injectable formulation having all of these limitations. Suzuki discloses microcapsules, and states that

> It is particularly preferred to use a microcapsule-dispersing medium which contains one or more compounds selected from the group consisting of hyaluronic acid, chondroitin sulfate, and salts thereof. The use of such a dispersion medium makes it possible to minimize irritation to the joint, which tends to occur as a result of administration (column 5, Lines 2-8).

Suzuki does not disclose, however, an injectable formulation as claimed, comprising hyaluronic acid dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight by volume. Consequently, claims 23, 25-28, and 34 are patentable over Cleland. Withdrawal of the rejection is respectfully requested.

35 USC § 103

Claims 17, 20-21, 23, 25-29, 34-35 and 39 were rejected under 35 USC § 103(a) as unpatentable over Cleland in view of page T515 of the Aldrich catalog (1996-1997). Claims 17, 21, 35, and 39 have been canceled. With respect to the remaining claims, the Applicants traverse this rejection.

The Applicants note that in an obviousness analysis,"[t]he teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the

prior art, and not based on applicant's disclosure." *MPEP 2142*. Applicants submit the claims are not rendered obvious by Cleland in view of the Aldrich catalog, because the references do not disclose all of the claim limitations, nor provide any suggestion or motivation to combine or modify the references to disclose all of the limitations.

Amended independent claim 20 recites a method for administering a biologically active agent, comprising injecting a formulation comprising hyaluronic acid dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight by volume, and particles comprising a biologically active agent and a biocompatible polymeric matrix. Claims 21, 35, and 39 depend from independent claim 22. Amended claim 22 recites an injectable formulation comprising hyaluronic acid dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight by volume, and particles comprising a biologically active agent and a biocompatible polymeric matrix.

The administration of polymer-based drug formulations is known to be problematic (paragraph bridging pages 2-3 of the application). Previously, excipients, surfactants, and salts have been added to reduce agglomeration or alter the particles' fluid properties (page 2 line 26 to page 3, line 2). Nevertheless, administration of the formulations through needles is difficult (page 3, lines 3-4).

The present specification discloses for the first time that the use of hyaluronic acid in the presently claimed concentration range improves injectability (Examples 3, 4, 5, and 7). Applicants have further demonstrated that use of hyaluronic acid in formulations for injection is superior compared to the use of other polymers, such as sodium alginate, dextran 70, jeffamine M-600, jeffamine ED-2001, keretan sulphate, poly-L-ornithine, xanthan gum, and gellan gum (Example 6).

In contrast, Cleland does not disclose or suggest an injectable formulation or a method for administering a biologically active agent as claimed. As discussed above, Cleland does not disclose an injectable formulation comprising hyaluronic acid dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight by volume. Nor does Cleland provide any motivation for selecting an injectable formulation comprising hyaluronic acid in the claimed range.

Page T515 of the Aldrich catalog does not remedy these deficiencies of Cleland. Aldrich merely discloses various gauge needles, and teaches nothing about any injectable formulation.

Applicants respectfully submit, therefore, that neither Cleland et al. nor the Aldrich catalog, alone or in combination, teach or suggest an injectable formulation as claimed. Withdrawal of the rejection is requested.

SUMMARY

Applicants submit that the claims are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicants' representative if prosecution may be assisted thereby.

Respectfully submitted,

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